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AF/1616

Docket No. 20257 US C038435/0110665 PATENT APPEAL

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Date: March 24, 2004

Sheila Chang

Sheila Chang

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)

David Carl BURDICK *et al.*)

Serial No.: 09/448,356)

Filed: November 23, 1999)

For: **PHYTOSTEROL AND/OR PHYTOSTANOL DERIVATIVES**)

Examiner: Sabiha Naim Qazi

Art Unit: 1616

New York, New York
March 24, 2004

APPELLANTS' BRIEF ON APPEAL

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Arlington, VA 22313-1450

Sir:

In accordance with 37 CFR §1.192(a), this brief is being submitted in triplicate, together with the required fee. 37 CFR §1.17(c).

The Notice of Appeal was accorded a filing date of August 27, 2003. A five-month extension of time to file this Brief on Appeal is hereby requested. Accordingly, this Brief is filed timely upon mailing, with an executed Certificate of Mailing, on or

before March 29, 2004, because March 27, 2004 is a Saturday. 35 USC §21(b); 37 CFR §§ 1.7, 1.8, 1.136, and 1.192(a).

Enclosed is a check in the amount of $2,340.00 to cover the fee for filing the Brief ($330.00) and the fee for the extension of time ($2,010.00). 37 CFR §1.17. Please charge any fees not otherwise paid by check to Deposit Account No. 02-4467. A duplicate copy of this sheet is enclosed.

IDENTIFICATION OF REAL PARTY IN INTEREST

The real party in interest is DSM NUTRITIONAL PRODUCTS, INC., which is the assignee of the present application and is a corporation organized and existing under, and by virtue of, the laws of the State of Delaware. Ownership of DSM NUTRITIONAL PRODUCTS, INC. lies in DSM N.V., a Dutch corporation.

RELATED APPEALS AND INTERFERENCES

Upon information and belief of the undersigned counsel, Appellants and the assignee are not aware of any pending appeals or interferences, which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

STATUS OF ALL CLAIMS AND AMENDMENTS

A. Status Prior To Final Rejection

As originally filed, the application contained claims 1-20. Claims 9-20 were withdrawn from prosecution in view of a restriction requirement imposed by the Examiner. [*See* Paper No. 2]. Subsequently, claim 1 was amended to specifically recite "eicosapentaenoic acid or docosahexaenoic acid;" claim 8 was amended to further clarify the "second ester;" claim 7 was cancelled; and claims 21-23 were added.

[*See* July 14, 2000 Response To Office Action Including Amendment]. For unexplained reasons, the Examiner withdrew newly added claims 21-23. [*See* Paper No. 6]. Amendments to claims 1 and 8 and additional claims 24 and 25 were presented in the Response To Office Action Under Rule 116 filed on November 20, 2001, but these amendments and additional claims were not entered. [*See* Paper No. 11].

A Rule 53 Continued Prosecution Application ("CPA") was filed on May 14, 2002 with a request to enter the amendments and additional claims presented in the November 20, 2001 Response. The amendments and added claims were entered by the Examiner. [*See* Paper No. 15]. Thus, claim 1 was amended to remove the recitation of "phytostanol" and to recite that the compound is "a liquid at temperatures from about -20°C to about 20°C." Claim 8 was amended to place it in independent form, to remove the recitation of "phytostanol," and to further clarify the "phytosterol ester compound" and the "second ester."

The specification was subsequently amended to recite the claim to benefit to EP 98122412.4 and EP 99119337.6 filed on November 26, 1998 and September 29, 1999, respectively. [*See* Response To Office Action Including Amendment dated January 27, 2003].

B. <u>Status After Final Rejection</u>

The Examiner issued a Final Rejection on April 23, 2003 (Paper No. 17) and Appellants filed a Notice of Appeal on August 25, 2003, which was received by the PTO on August 27, 2003. An Amendment is being filed concurrently herewith canceling claims 5 and 6, without prejudice, to reduce issues on appeal. 37 CFR §116(b).

C. Identification Of Claims On Appeal

Claims 1-4, 8, 24, and 25 are on appeal and are reproduced in APPENDIX I to this brief.

SUMMARY OF THE INVENTION AND THE CLAIMS

Arteriosclerosis is a leading cause of death in many parts of the Western world. It has been shown that low-density lipoprotein (LDL) cholesterol is directly associated with the development of cardiovascular disease; whereas high-density lipoprotein (HDL) cholesterol has an inverse relationship with cardiovascular disease development. People with combined hyperlipidemia run increased risks of heart disease. Elevated blood serum levels of cholesterol and elevated levels of triglycerides are generally accepted as both causes and indicators of the progression of cardiovascular disease. Thus, lowering serum cholesterol and triglyceride levels is a desirable goal and a major strategy for intervention. [Specification, page 1, line 23 – page 2, line 5].

The claims on appeal are directed to various phytosterol and phytostanol ester compounds and compositions having a fatty acid component from eicosapentaenoic acid ("EPA") or docosahexaenoic acid ("DHA"). [*See* Claims 1-4, 8, 24 and 25]. These compounds/compositions are useful for lowering ***both*** plasma cholesterol and triglyceride levels and, thus, positively affect two of the major risk factors for cardiovascular disease in humans. [Specification, page 5, lines 1-12].

By way of background, phytosterols are plant sterols found, for example, in small amounts in vegetable oils, such as, corn, bean, or other plant oils, where they occur as free sterols, fatty acid esters and glycosides. Phytosterols are structurally similar to cholesterol, the main differences occurring in the carbon skeleton of their side chains. A

number of different phytosterol structures are found in nature. The most common of these structures are campesterol, β-sitosterol, and stigmasterol. Reduction of a phytosterol yields a saturated phytosterol, called a phytostanol, such as campestanol or sitostanol, which also occur naturally in small amounts. A normal human diet typically leads to ingestion of less than one-half gram a day of such substances in various forms. [*Id.*, page 1, lines 8-16].

It is known that ingestion of phytosterols and/or phytostanols in defined amounts (*e.g.*, several grams a day or more) may reduce blood serum cholesterol levels. It is assumed that free phytosterols and phytostanols inhibit the uptake of dietary and biliary cholesterol through displacement of cholesterol. In general, only modest reductions of serum cholesterol levels have been observed by adding free phytosterols or phytostanols to the diet. [*Id.*, page 1, lines 17-22].

In view of the foregoing, methods for lowering serum cholesterol levels have been proposed. Such methods include administering phytosterols in various forms to a patient. Similarly, methods for lowering serum triglycerides have been proposed. These methods include administering a polyunsaturated fatty acid ("PUFA") to a patient. [*Id.*, page 2, line 20 - page 3, line 25].

Conventional therapies used free phytosterols to lower plasma cholesterol levels. One problem encountered by these conventional methods was the crystalline nature of the phytosterol and its low solubility. These properties of free phytosterol limited the amount of the compound that could be incorporated into a food, such as, an oil or a butter, and thus limited the amount of the phytosterol that could be delivered to a patient. [*Id.*, page 2, lines 15-19].

To solve these limitations imposed by the physical properties of free phytosterol, phytosterol esters of various fatty acids have been used to deliver higher quantities of phytosterol to patients. These conventional compounds, compositions and processes, however, suffer from the drawback that they are focused exclusively on delivering a pharmaceutically appropriate amount of a phytosterol to a patient. None of these compounds, compositions or methods describe lowering ***both*** serum cholesterol and triglyceride levels. [*Id.*, page 2, line 28 - page 3, line 25].

These drawbacks are overcome by the presently claimed invention, which provides a phytosterol or phytostanol ester made from two specific PUFAs – EPA and DHA – having plasma triglyceride-lowering properties. Such compounds and compositions have the effect of lowering ***both*** plasma cholesterol and triglyceride levels. [*Id.*, page 5, lines 2-12].

For example, in one embodiment, the claimed invention provides a phytosterol or a phytostanol ester compound produced from a reaction of a phytosterol or a phytostanol with EPA or DHA, the compound being liquid at temperatures from about -20°C to about 20°C. [*Id.*, Claims 1 and 24; page 3, lines 27-30; page 5, lines 2-7; and page 13, line 18 – page 14, line 11].

In a preferred embodiment, the phytosterol is selected from β-sitosterol, stigmasterol, campesterol and mixtures thereof. [*Id.*, Claims 2 and 3; and page 11, line 31 - page 12, line 1]. More preferably, the phytosterol is β-sitosterol. [*Id.*, Claim 4; and page 12, line 1].

The claimed invention also provides a composition containing an admixture of a phytosterol ester compound, which is produced from a reaction of a phytosterol with

EPA or DHA; and "a second ester, which is the product of an esterification reaction between a phytosterol and/or a phytostanol and (i) a fatty acid having less than 18 or more than 22 carbon atoms and at least three carbon-carbon double bonds and/or; (ii) a fatty acid having from 18 to 22 carbon atoms and less than three carbon-carbon double bonds." [*Id.*, Claim 8; page 4, lines 1-8; and page 12 lines 4-6].

Another embodiment of the present invention provides a compound produced from a reaction of EPA or DHA with "a mixture of phytosterol and phytostanol, wherein the phytosterol is selected from the group consisting of β-sitosterol, stigmasterol, campesterol and mixtures thereof; and the phytostanol is selected from the group consisting of campestanol, β-sitostanol and mixtures thereof." [*Id.*, Claim 25; page 3, lines 27-30; page 5, lines 2-7; and page 11, line 31 – page 12, line 3].

STATEMENT OF THE REJECTIONS AND ISSUES

Whether claim 8 is unpatentable under 35 USC §103(a) over Mitchell, U.S. Patent No. 4,588,717 ("Mitchell"), U.S. Patent No. 4,879,312 ("Kamarei") and Miettinen *et al.*, WO 92/19640 ("Miettinen"). [Paper No. 17 at 3].

Whether claims 1-4, 24 and 25 are unpatentable under 35 USC §103 over Miettinen in view of Mitchell. [*Id.* at 6].

GROUPING OF CLAIMS

Not all claims stand or fall together. Arguments are presented below which demonstrate the patentability of claim 8. Separate arguments are presented which demonstrate the separate patentability of claims 1-4. Separate arguments are presented which demonstrate the separate patentability of claims 24 and 25.

SUMMARY OF THE DISCLOSURES OF THE REFERENCES

A. Mitchell

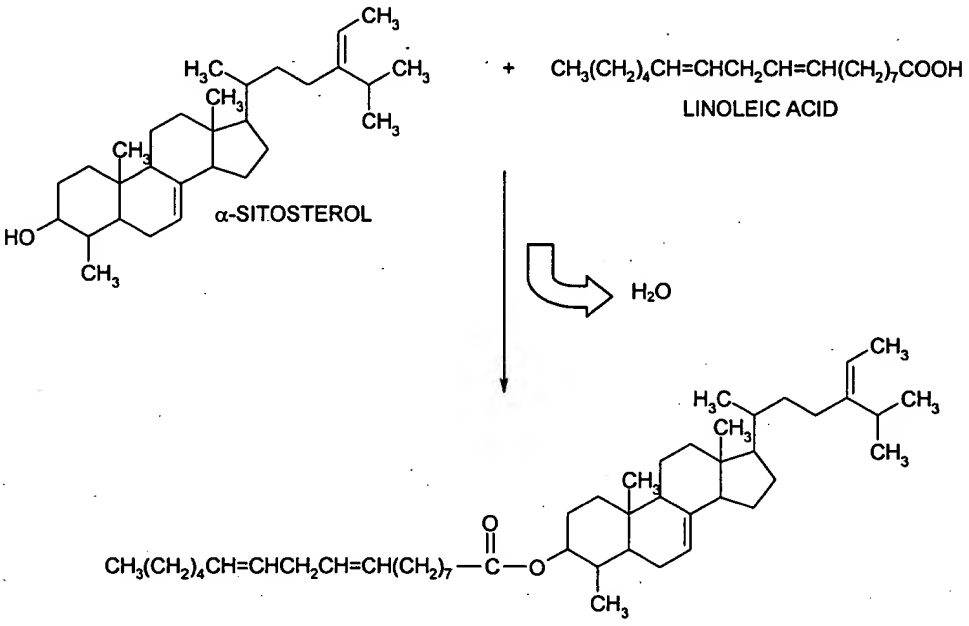
Mitchell discloses a broad range of vitamin supplements containing phytosterol esters, substituted fructose compounds and antitrypsin enzymes, as well as, methods of making same. [Mitchell, Column 1, lines 7-12]. The disclosed phytosterol ester supplements are designed to provide a "method for administering steroids and hormones to humans and other animals without directly introducing the hormones and steroids into the blood stream or digestive tract," which would have undesirable effects, including androgenic effects, acne, voice changes, poor absorption and the generation of toxic byproducts, *etc.* [*Id.*, lines 46-65].

Mitchell broadly discloses fatty acid esters of phytosterols, such as sitosterol, stigmasterol, taraxasterol and mixtures thereof. [*Id.*, Column 3, lines 26-36; and Column 5, lines 48-51]. Mitchell broadly defines the phytosterol portion of the disclosed esters to include "all phytosterols" and derivatives thereof. [*Id.*, Column 5, lines 26-28].

Mitchell defines the fatty acid portion of the disclosed esters to include "***any*** fatty acid having from about 18 to about 20 carbon atoms in the main carbon chain and at least two carbon-to-carbon double bonds, in addition to terminal carboxyl and methyl groups." (emphasis added) [*Id.*, Column 6, lines 2-8]. Mitchell recognizes that "many fatty acids are included within this category." [*Id.*]. In preferred embodiments, Mitchell identifies linoleic acid (C_{18}, ω-6-fatty acid), linolenic acid (C_{18}, ω-3-fatty acid) and archidonic acid (C_{20}, ω-6-fatty acid) as the fatty acid source of the phytosterol esters. [*Id.*, Column 3, lines 26-36]. Mitchell further includes fatty acids having less than 18 carbon atoms and more than 20 carbon atoms within the scope of the invention, but notes that phytosterol esters made with such fatty acids "tend to have less utility in

achieving the purposes of the present invention" (*i.e.*, delivering steroid and hormone precursors to the body). [*Id.*, Column 6, lines 9-15].

Mitchell describes the reaction between a phytosterol and a fatty acid as a "condensation" reaction and provides a characteristic reaction scheme, which is said to be "essentially the same" reaction between "any given phytosterol" and "any given fatty acid."

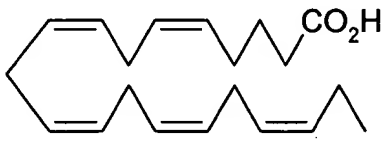


[*See Id.*, Column 8, lines 33-37 and Equation 1].

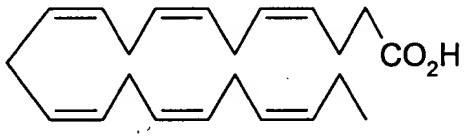
Mitchell provides 75 examples of the phytosterol ester vitamin supplement. In those examples, however, only three different fatty acids are exemplified as part of the phytosterol ester – linoleic acid (Examples 1-25), linolenic acid (Examples 26-50), and arachindonic acid (Examples 51-75). Likewise, in the 75 examples, only three phytosterols are exemplified as the phytosterol component of the ester – sitosterol, stigmasterol and taraxasterol.

B. Kamarei

Kamarei discloses a "method for provoking or enhancing" the formation of new blood vessels, a process called "angiogenesis," in a patient by administering "an angiogenically effective amount of an angiogenically active ω-3 polyunsaturated fatty acid." [Kamarei, Column 3, lines 13-17]. Kamarei discloses that "preferred" ω-3 polyunsaturated fatty acids are EPA and DHA. [*Id.*, lines 18-19.]. Kamarei sets forth the chemical structures of EPA and DHA in Fig. 1:



EPA



DHA

Kamarei discloses that a diet rich in *ω*-3 fatty acids has a beneficial effect in humans, including reduction of plasma cholesterol and triglyceride levels. [*Id.*, Column 2, lines 39-41]. Kamarei also observes that EPA reportedly was known to reduce triglyceride and very low density lipoprotein ("VLDL") serum levels. But, when administered to a patient, EPA caused bleeding time to increase and the ability of platelets to aggregate to decrease. [*Id.*, lines 54-59]. Kamarei also discloses that it was known to use of a combination of one of EPA and DHA and a linoleic acid derivative in the treatment of thrombo-embolic conditions. [*Id.*, lines 63-68]. Kamarei also discloses

that it was known to administer "mixtures of EPA and DHA/linoleic acid derivatives ... in food form." [*Id.*, Column 3, lines 2-5].

C. Miettinen

Miettinen discloses β-sitostanol fatty acid ester compounds and mixtures, which lower serum cholesterol levels. [*See* Miettinen, Abstract; and page 6, lines 8-34]. Miettinen discloses that a β-sitostanol mixture is esterified with "different fatty acid ester mixtures by a commonly known chemical interesterification technique." [*Id.*, page 6, lines 26-30]. Miettinen further discloses that the β-sitostanol fatty acid esters may be added to food and convey advantages in "national nutrition and in the treatment of hypercholesterollemia." [*Id.*, page 8, lines 30-34].

Miettinen also discloses that the described compounds/mixtures have wide applications because their physical properties may be modified easily by altering the fatty acid composition of the mixture. Miettinen further discloses that "the fatty acid composition of the β-stanol fatty acid ester mixture can be selected so as to contain large amounts of monoenes and polyenes, whereby its efficacy in lowering the cholesterol levels in serum are enhanced." [*Id.*, page 9, lines 21-30].

In addition to mixtures of rapeseed oil, Miettinen discloses that a methyl ester or a mixture of methyl esters of any vegetable oil, "especially" C_{2-22} fatty acids from a vegetable oil, may be used to esterify the β-sitostanol. [*Id.*, page 10, lines 20-24; *see also* page 6, lines 33-34].

SUMMARY OF THE POSITIONS TAKEN BY THE EXAMINER IN THE FINAL OFFICE ACTION

In the final Office Action, the Examiner made two rejections under §103(a). Both rejections rely, at least, on Mitchell and Miettinen. [*See* Paper No. 17 at 3 and 6].

A. Rejection 1

In the first rejection, the Examiner rejected claim 8 over Mitchell, Kamarei and Miettinen. In making this rejection, the Examiner asserted that Mitchell discloses "vitamin supplements containing phytosterol esters such as fatty acid esters of sterol, stigma sterol [sic] and taxasterol, in various combinations." [*Id.* at 3]. The Examiner also asserted that Mitchell discloses that "[f]atty acid[s] hav[ing] about 18-20 in addition to two carbon atoms of terminal carboxyl and methyl groups (lines 2-15, col. 6) and at least two double bonds such as arachidonic acid, linoleic acid and linolenic acids are used to make phytosterol esters (see lines 21-58, col. 3; lines 43-65, col. 5; equation 1 and lines 1-11 in col. 8)." [*Id.*]. The Examiner also asserted that Mitchell discloses that "the reaction between any given phytosterol and any given fatty acid is essentially the same...." [*Id.*].

The Examiner asserted that Kamarei discloses "that a diet rich in omega-3-fatty acids has beneficial effects in humans...." [*Id.* at 4]. The Examiner also asserted that Kamarei discloses that "one of n-3 PUFA *i.e.* eicosapentaenoic acid (EPA) and DHA reduces triglyceride and very low-density lipoprotein (VLDL) serum levels and reduces whole blood viscosity." (emphasis in original) [*Id.*].

The Examiner asserted that Miettinen discloses "a composition of β-sitostanol fatty acid ester mixture or fatty acid ester mixture" and that the "physical properties of mixture can be modified easily by altering the fatty acid composition of the mixture." [*Id.*]. The Examiner further asserted that Miettinen discloses a "fatty acid mixture containing 2-22 carbon atom and esterification of sitostanol." [*Id.*].

The Examiner acknowledged, however, that claim 8 differs from the cited documents in claiming a "phytosterol ester compound produced by the reaction of a phytosterol and two specific fatty acids" – EPA (a C_{20}, ω-3-fatty acid) and DHA (a C_{22}, ω-3-fatty acid). [*Id.* at 5]. The Examiner asserted that "it ***would be*** obvious to ... employ" a phytosterol composition in combination with an ω-3-fatty acid becase these agents "***are known*** individually" for lowering plasma cholesterol and triglyceride levels. (emphasis added) [*Id.*]. The Examiner concluded that claim 8 is nothing more than a combination of prior art teachings:

> Instant claim ***is*** a selection of prior art teachings as EPA and DHA contain 20 and 22 carbons respectively which is taught by the prior art .... (emphasis added) [*Id.*].
>
> * * * *
>
> All ingredients of the instant invention ***are*** taught by the prior art for the same use. [*Id.* at 6].
>
> * * * *
>
> The combination of agents, each of which known for the same purpose, ***is*** considered *prima facie* obvious. (emphasis added) [*Id.*].

The Examiner asserted that the "motivation" apparently to combine Mitchell, Kamarei and Miettinen flows generally from "the prior art."

> Motivation ***is to prepare*** additional beneficial composition of sterols with unsaturated fatty acids such as omega-3-fatty acids, EPA, DHA, useful for lowering the cholesterol and triglyceride levels, because this use has been taught by the prior art for the said compositions. Preparation of supplemental vitamins, margarine and mayonnaise is taught by the prior art cited above. (bold emphasis added) [*Id.*].

B. Rejection 2

In the second rejection, the Examiner rejected claims 1-6, 24 and 25 over the "combined teachings" of Miettinen and Mitchell. [*Id.* at 6]. In making the rejection with respect to claims 1-6, 24 and 25, the Examiner relied on substantially the same summaries of Miettinen and Mitchell set forth in the earlier rejection of claim 8. [*Id.* at 6-7]. The Examiner acknowledged, however, that the rejected claims differed from Miettinen and Mitchell in the recitation of "specific fatty acids" – EPA and DHA. [*Id.* at 7-8]. Again, the Examiner characterized the rejected claims as nothing more than a "selection of prior art teachings."

> Instant claims are a selection of prior art teachings. [*Id.* at 8].

The Examiner then concluded that it would have been obvious to make the claimed compounds/compositions by making the appropriate selection of fatty acids based on the "ample motivation" provided by the "prior art."

> It ***would have been*** obvious to one skilled in the art to prepare additional beneficial composition by selecting any fatty acids for example, docosahexaenoic acid and eicosahexaenoic acid from fatty acid 2-22 carbon atoms taught by the prior art. There has been ***ample motivation*** provided by the prior art to prepare the instant invention. Instant compositions ***would have been*** obvious at the time of invention. The subject as instantly claimed ***would have been*** obvious to one at the time of invention. (emphasis added) [*Id.*].[1]

1/ We note that the rejection refers to "eicosahexaenoic acid," we assume, however, that the Examiner intended "eicosapentaenoic acid." If this assumption is incorrect, we request that the Examiner confirm on the record that "eicosahexaenoic acid" was intended.

THE LEGAL STANDARD

To reject a claim under 35 USC §103, an examiner must show an unrebutted *prima facie* case of obviousness. *In re Deuel*, 34 USPQ2d 1210, 1214 (Fed. Cir. 1995). Obviousness must be based upon facts. *Ex parte Saceman*, 27 USPQ2d 1472, 1474 (BPAI 1993). When a conclusion of obviousness is not based on facts, it cannot stand. *Ex parte Porter*, 25 USPQ2d 1144, 1147 (BPAI 1992).

In combining references, the suggestion and motivation to make the combination must be based on "actual evidence" that must be "clear and particular." *In re Dembiczak*, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) *abrogated on other grounds by In re Gartside*, 53 USPQ2d 1769 (Fed. Cir. 2000). Moreover, "when the PTO asserts that there is an explicit or implicit teaching or suggestion in the prior art, it must indicate where such a teaching or suggestion appears in the reference." *In re Rijckaert*, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) *citing In re Yates*, 211 USPQ 1149, 1151 (CCPA 1981).

In the absence of a *prima facie* case of obviousness, an applicant who complies with the other statutory requirements is entitled to a patent. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002); and *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On appeal to the Board, an applicant can overcome a rejection by showing insufficient evidence of *prima facie* obviousness. *Oetiker*, 24 USPQ2d at 1444.

SUMMARY OF THE ARGUMENT

The Examiner has failed to meet her burden of setting forth a *prima facie* case of obviousness. Rejections 1 and 2 are both legally and factually deficient, and, therefore, cannot stand.

In making Rejections 1 and 2, the Examiner relied on a "selection of prior art teachings" standard that is inconsistent with the statute, legal precedent, and the PTO's own rules. Rejection 1 is also legally deficient because the Examiner conducted the analysis at the time she wrote the rejection - she did not go back in time to just prior to the date of invention and conduct the analysis as she was required to do. Rejections 1 and 2 are further legally deficient because neither of them identify where the motivation to make the proposed combinations is found. At best, the rejections rely on broad assertions – without any evidence – that the motivation "is taught by the prior art" or that "ample motivation [is] provided by the prior art."

Even if the cited documents are combined in the manner suggested by the Examiner in Rejections 1 and 2, there is still a gap, namely that none of the cited documents disclose or suggest the use of the specifically claimed EPA and DHA PUFAs to make a phytosterol ester. Thus, both rejections are factually deficient.

Lastly, the Examiner completely ignored claims 24 and 25. The Examiner failed to carry out the *Graham v. John Deere* analysis for these claims. She did not determine the scope of the claims, nor did she compare the scope of the claims to the cited art. Thus, the rejection of claims 24 and 25 is not based on any legal or factual analysis and must be reversed.

ARGUMENT

POINT I

THE EXAMINER RELIED ON A "SELECTION OF PRIOR ART TEACHINGS" STANDARD THAT FALLS SHORT AND IMPERMISSIBLY SHIFTS THE BURDEN TO APPELLANTS

The first error is that in both Rejections 1 and 2, the Examiner dismissed the claims as simply "a selection of prior art teachings." [Paper No. 17 at 5 and 6 (Rejection 1) and at 8 (Rejection 2)]. With respect to Rejection 1, the Examiner concluded:

> Instant ***claim is a selection of prior art teachings*** as EPA and DHA contain 20 and 22 carbons respectively which is taught by the prior art .... (emphasis added) [*Id.* at 5].
>
> * * * *
>
> All ingredients of the instant invention are taught by the prior art for the same use. [*Id.* at 6].

With respect to Rejection 2, the Examiner was similarly dismissive of the rejected claims:

> Instant ***claims are a selection of prior art teachings.*** (emphasis added) [*Id.* at 8].

Whether or not a claimed invention can be selected from among various pieces of prior art, however, misses the point. In fact, most inventions ***are*** combinations of old elements. If the Examiner's "selection of prior art teachings" were the correct standard, very few applications would issue as patents. Unfortunately for the Examiner, her standard has been expressly repudiated by the Board, as well as, the Federal Circuit.

> As this court has stated, 'virtually all [inventions] are combinations of old elements....' If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, ***rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be 'an illogical and inappropriate process by which to determine patentability.'*** *In re Rouffet*, 47 USPQ2d 1453, 1457 (Fed. Cir. 1998) (internal citations omitted) (emphasis added).

See also Ex parte West, 2003 WL 23013115, *2 (BPAI 2003) (unpublished) (reversing §103 rejection because it failed to show why one would be motivated to combine two elements found in the prior art to arrive at the claimed chewing gum base) and *Ex parte Sterner*, 1995 WL 1696874, *2 (BPAI 1995) (unpublished) (reversing §103 rejection for using Appellant's specification as a blueprint to combine prior art).

The linchpin of the Examiner's position is that Mitchell and Miettinen disclose or suggest incorporating EPA or DHA into a phytosterol ester. To support this position in Rejection 1, the Examiner cited specifically to "lines 20-25 on page 10 of WO '640" (Miettinen) and generally to "US '717" (Mitchell). [Paper No. 17 at 5]. Likewise, in Rejection 2, the Examiner observed generically that "the prior art teaches the reaction product of phytosterol with fatty acids especially containing approximately 2-22 carbon atoms." [*Id.* at 8].

The problem with the Examiner's reasoning in both rejections is two-fold. First, the citation to Miettinen in Rejection 1 actually discloses methyl esters or mixtures thereof from "***any*** vegetable oil, especially of fatty acids which contain approximately 2-22 carbon atoms." (emphasis added) [Miettinen, page 10, lines 20-25]. Thus,

Miettinen does not disclose or suggest what the Examiner says it does, namely EPA and DHA. Rather, at best, Miettinen discloses a genus of fatty acids that contain "approximately 2-22 carbon atoms." [*Id.*]. The Examiner failed to identify where in Miettinen that EPA or DHA are specifically identified or even suggested as being good choices.

Second, with respect to Mitchell, the Examiner failed to cite to a specific portion of the patent, instead telling us to see "US '717." [Paper No. 17 at 5]. Notwithstanding the lack of specificity of the rejection, we note that Mitchell also does not disclose or suggest what the Examiner says it does, namely EPA and DHA. Rather, Mitchell discloses reacting a phytosterol with essentially ***any*** fatty acid. Mitchell does specifically identify fatty acids having from "about 18 to about 20 carbon atoms," such as for example, "linoleic acid," "linolenic acid," and "arachidonic acid." [*See e.g.*, Mitchell, Column 5, lines 55-66]. But, Mitchell also discloses that fatty acids "having less than 18 carbon atoms" or "more than 20 carbon atoms ... may be used."[2/] [*Id.*, Column 6, lines 9-15]. Here too, the Examiner failed to identify where in Mitchell EPA or DHA are specifically identified or even suggested as being good choices.

Tellingly, in Rejection 1, when the Examiner was applying her "selection of prior art teaching" standard, she did not mention Kamarei, the only cited document that does specifically name EPA and DHA. [*See* Paper No. 17 at 5]. We submit that this omission was predicated on the Examiner's recognition that Kamarei, as a whole, is directed to "provocation or enhancement" of blood vessel growth (angiogenesis). Thus, one skilled in the art would not look to combine such a document with Mitchell or

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[2/] We acknowledge Mitchell discloses that fatty acids having less than 18 or more than 20 carbon atoms "tend to have less utility." Nevertheless, Mitchell fairly conveys that ***any*** fatty acid may be used, albeit with varying levels of utility. [*See* Mitchell, Column 6, lines 9-15].

Miettinen, which disclose cholesterol lowering effects of various phytosterol esters.

In sum, we respectfully submit that Rejections 1 and 2 – ***not*** the claims – are based on a "selection of prior art." [Paper No. 17 at 5 and 8]. The problem, as recognized by the Board and Federal Circuit, is that Rejections 1 and 2, like those in *Rouffet*, *West*, and *Sterner*, are devoid of any evidence to explain why one skilled in the art would make the particular selections proposed by the Examiner. Why would one have selected DHA or EPA based on the generic disclosure of ***any*** C_{2-22} fatty acid in Miettinen? Why would one have selected DHA or EPA based on the generic disclosure of ***any*** fatty acid in Mitchell or preferred fatty acids having about 18 to about 20 carbon atoms as exemplified by linoleic acid, linolenic acid, and arachidonic acid? Why would one have even considered DHA - a fatty acid containing 22 carbon atoms and within the scope of Miettinen - when Mitchell teaches that such compounds are not as useful as C_{18-20} fatty acids?

Without such evidence, the only conclusion is that the Examiner used Appellants' specification as a blueprint to navigate from disclosures of "any fatty acid," C_{2-22} fatty acids, and C_{18-20} fatty acids cited in the documents applied by the Examiner to EPA and DHA as claimed. But, that is exactly the kind of hindsight reconstruction that is not permitted. *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531-1532 (Fed. Cir. 1988) ("There must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from applicant's disclosure."); *In re Bond*, 15 USPQ2d 1566, 1568-1569 (Fed. Cir. 1990) (The Board's holding "does not reflect the admonition of this court that '[o]bviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or

incentive supporting the combination.' The Board's analysis is a classic case of hindsight reconstruction of the claimed invention."); *Ex parte Bertelloti*, 2004 WL 77114, *2 (BPAI 2004) (unpublished) ("In order to establish a *prima facie* case of obviousness, the examiner must show that some objective teaching, suggestion or motivation in the applied prior art taken as a whole and/or knowledge generally available to one of ordinary skill in this art would have led that person to the claimed invention as a whole, including each and every limitation of the claims, without recourse to the teachings in appellants' disclosure."); and MPEP §2141.03 8th Ed., Rev. 1, at 2100-124 ("The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure."). For this reason alone Rejections 1 and 2 should be withdrawn.

POINT II

THE EXAMINER IMPROPERLY CONDUCTED THE REJECTION 1 ANALYSIS AT THE TIME SHE WROTE THE REJECTION

Another error is that Rejection 1 carries out its limited analysis from the vantage point of one skilled in the art *circa* April 2003, namely, at the time the rejection was made, not just prior to the date the invention was made, as required by the statute, binding Federal Circuit precedent, and the PTO's own rules. *See* 35 USC §103(a); *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988) *quoting Panduit Corp. v. Dennison Mfg. Co.*, 1 USPQ2d 1593, 1595-96 (Fed. Cir. 1987) ("To reach a proper conclusion under §103, the decision maker ***must*** step backward in time and into the shoes worn by [a person having ordinary skill in the art] when the invention was unknown and just before it was made.") (emphasis added); and MPEP §2142 at 2100-123 ("To reach a proper

determination under 35 USC §103, the examiner ***must*** step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made.") (emphasis added).

The analysis for Rejection 1 carried out by the Examiner was conducted based on knowledge at the time the ***rejection*** was made. The Examiner stated that the "[i]nstant claim ***is*** a selection of prior art teachings...." [Paper No. 17 at 5]. The Examiner also stated that "it would ***be*** obvious ... to employ phytosterols composition [sic] in combination with omega-3-fatty acids ... because these agents ***are*** known individually for the treatment of the same disorderds." [*Id.*]. The Examiner also stated that "[t]he combination of agents, each of which ***is*** known for the same purpose, ***is*** considered *prima facie* obvious." [*Id.* at 6]. And, the Examiner asserted that "[m]otivation ***is*** to prepare additional beneficial composition of sterols with unsaturated fatty acids ...." [*Id.*].

The Examiner's analysis unmistakably uses verb forms of the present and present perfect tenses – "is," "would be" and "are known." The record is clear – the Examiner analyzed the claims from the vantage point of when she wrote the rejection. This is error. *See Fine*, 5 USPQ2d at 1598. Whether claim 8 "***is*** a selection of prior art teachings," whether claim 8 "would ***be*** obvious" because phytosterols and fatty acids "***are*** known individually for the treatment of the same disorders," whether a combination of agents "***is*** considered *prima facie* obvious" and whether the "[m]otivation ***is*** to prepare [a] beneficial composition" ***are all*** irrelevant questions to a determination under §103. What the Examiner was required to do, but did not do, was to go back in time to

just before the invention was made, and consider what one skilled in the art "would have known" based on Mitchell, Kamarei and Miettinen.

That the Examiner used a stock concluding paragraph correctly characterizing when the analysis should have taken place serves only to highlight that the analysis in Rejection 1 was impermissibly carried out at the wrong time. [*See* Paper No. 17 at 6]. Moreover, the verb tenses used in Rejection 2 stand in stark contrast to Rejection 1:

> It ***would have been*** obvious to one skilled in the art to prepare additional beneficial composition [sic] by selecting any fatty acids for example, docosahexaenoic acid and eicosahexaenoic acid from fatty acid 2-22 carbon atoms taught by the prior art. There has been ample motivation provided by the prior art to prepare the instant invention. Instant compositions ***would have been obvious at the time of invention***. The subject instantly claimed ***would have been*** obvious to one at the time of invention. (emphasis added) [Paper No. 17 at 8].[3/]

Thus, the Examiner clearly understood when a §103 analysis should have been conducted. Just as clearly, the Examiner did ***not*** go back in time in Rejection 1 to carry out the analysis. Because the Examiner failed to conduct the obviousness analysis of Rejection 1 from the vantage point of one skilled in the art just prior to the time the invention was made, the rejection of claim 8 should be reversed for this reason as well.

POINT III

THE EXAMINER FAILED TO IDENTIFY ANY SUGGESTION OR MOTIVATION TO COMBINE THE DOCUMENTS IN THE MANNER PROPOSED

Another error is that the Examiner failed to identify where in the cited documents of Rejection 1 (Mitchell, Kamarei, and Miettinen) and Rejection 2 (Miettinen and

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3/ See note 1 *supra*.

Mitchell) the motivation to combine them in the manner suggested is found.[4/] Because the Examiner failed to identify such evidence, she has not met her burden and the rejections should be reversed.

In Rejection 1, the Examiner's apparent basis for the required motivation rests solely on two sentences containing an unsupported allegation that one would be motivated to prepare "additional beneficial composition[s] of sterols."

> Motivation is to prepare additional beneficial composition [sic] of sterols with unsaturated fatty acids such as omega-3-fatty acids, EPA, DHA, useful for lowering the cholesterol and triglyceride levels, because this use has been taught by the prior art for the said compositions. Preparation of supplemental vitamins, margarine and mayonnaise is taught by the prior art cited above. (emphasis in original) [Paper No. 17 at 6].

The Examiner failed to cite with specificity to any of the three documents asserted in the rejection, relying instead on generalized statements attributed to "the prior art." Thus, Appellants and the Board are left to guess at the source, if any, of the motivation. As is well settled, however, the Examiner was required to conduct a thorough and searching factual inquiry into whether to combine the cited references. *See McGinley v. Franklin Sports, Inc.*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). The Examiner was also required to specifically identify the basis for her assertion of motivation. *In re Lee*, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) ("The need for

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4/ We note that Rejection 1 is ambiguous in that it is not clear whether the Examiner intended to reject claim 8 based on the three cited documents individually or in combination (*i.e.*, Mitchell in view of Kamarei and Miettinen). The rejection specifically identifies the three documents in the first paragraph [Paper No. 17 at 3], but then generically refers to the "prior art" [*Id.*] and the "reference" [*Id.* at 5] throughout the rest of the rejection interspersed with specific and generic citations to the cited documents. At bottom, Appellants are unfairly left to guess at the scope of the rejection. This ambiguity alone is sufficient to reverse the rejection. Out of an abundance of caution and to expedite the appeal process, we treat the rejection as if it were a combination, *i.e.*, Mitchell in view of Kamarei and Miettinen. We note, however, that even if considered separately, none of the cited documents alone are sufficient to render claim 8 obvious.

specificity pervades this authority."); *see also In re Rouffet*, 47 USPQ2d at 1459 ("The Board must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious."). The Examiner's burden in this regard is met only by showing evidence from the prior art or generally available knowledge that would lead one to make the proposed combinations. *In re Fritch*, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992).

In Rejection 1, the Examiner failed to identify where in Mitchell, Kamarei and Miettinen there is a disclosure or suggestion that a phytosterol ester made from EPA or DHA would be useful for any purpose. Indeed, the Examiner completely ignored the disclosure in Kamarei that administration of EPA - not even an ester of EPA - caused undesirable side effects, such as, increased bleeding time and decreased platelet aggregation. [*See* Kamarei, Column 2, lines 56-59].

Moreover, the Examiner omitted any explanation of why Kamarei is even combinable with Mitchell and Miettinen. In this regard, we note that Kamarei, as a whole, is directed to promoting/enhancing angiogenesis - not treating high cholesterol levels using various phytosterol esters as described in Miettinen or administering steroid and hormone precursors using various phytosterol esters as set forth in Mitchell. Thus, it was the Examiner's burden to explain why one skilled in the art would look to an angiogenesis paper when confronted with determining which fatty acid to react with a phytosterol to produce a phytosterol ester compound. This the Examiner did not do.

The Examiner's analysis of the motivation to select and combine various teachings from Mitchell, Kamarei and Miettinen should have been "thorough and searching"; it should have made with "specificity"; and it should have been explained

with "evidence." Instead, the Examiner relied solely on the two sentences quoted above and on *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980), to explain her basis of motivation. Both sentences cite generally to "the prior art." [*See* Paper No. 17 at 6]. Neither sentence identifies any of the three cited documents by name or where to look for the evidence that is supposedly found therein. [*Id.*]. And, the Examiner completely ignores evidence in Kamarei that undermines her suggestion that "the prior art" provides a motivation to use EPA in a phytosterol - namely the observation that EPA is known to cause increased bleeding time and decreased platelet aggregation. [*Id.*].

The Examiner's reliance on *Kerkhoven* is also to no avail. In *Kerkhoven*, the CCPA held that the mere mixing together of two known detergent components in a process for preparing a detergent composition, without more, was obvious. 205 USPQ at 1072. Those are not the facts here. The present claims are directed to compounds, not processes as recited in *Kerkhoven*. Moreover, here the claimed phytosterols and phytostanols are chemically reacted with EPA and DHA – they are not simply mixed together as in *Kerkhoven*. Moreover, here one of the cited documents – Kamarei – specifically discloses that EPA has negative side effects (*i.e.*, increased bleeding time and decreased platelet aggregation).

Indeed, the present case is much like the facts in *Ex parte Bokisa*, wherein the Board distinguished *Kerkhoven* and reversed a §103 rejection, in part, because the claimed invention was not merely a mixing together of known compositions and, in part, because the cited art taught away from the claimed invention. See 1997 WL 1897871, *2 -*3 (BPAI 1997) (unpublished); *See also Ex parte Garfield*, 2004 WL 77127, *3 (BPAI

2004) (unpublished) (distinguishing *Kerkhoven* and reversing a § 103 rejection because the cited art failed to disclose all of the elements recited in the rejected claims).

In short, the Examiner's two sentence basis for motivation and her reliance on *Kerkhoven* are insufficient to meet her burden. Accordingly, Rejection 1 should be reversed for this reason as well.

Compared to Rejection 1, Rejection 2 is even less compliant with the obligations regarding a showing of motivation. In Rejection 2, the Examiner's sole basis for the required motivation rests on a nebulous assertion of "ample motivation provided by the prior art."

> There has been ample motivation provided by the prior art to prepare the instant invention. [*Id.* at 8].

Here too, the Examiner cites only to the "prior art" generally for the motivation to combine the disclosures of Miettinen and Mitchell. Attributing the alleged "ample motivation" to the "prior art," without more, is not the kind of thorough and searching analysis required by *McGinley*. An allegation that the prior art provides "ample motivation," without more, is not the kind of specificity demanded by *Lee*. And, reliance on an allegation of "ample motivation" avoids the requirement for evidence commanded by *Fritch*. At bottom, the Examiner's single sentence basis for motivation is insufficient to meet her burden. Accordingly, Rejection 2 should be reversed for this reason as well.

POINT IV

THE EXAMINER MISINTERPRETED THE SCOPE OF THE CITED DOCUMENTS AND OVERLOOKED A FACTUAL GAP IN THE REJECTIONS

Another error is that the Examiner misconstrued the scope of Mitchell and Miettinen as applied in Rejection 2. The Examiner acknowledged in Rejection 2 that Mitchell and Miettinen did not specifically disclose EPA and DHA recited in claims 1-4, 24 and 25. [Paper No. 17 at 7-8]. The Examiner asserted, however, that Mitchell and Miettinen disclosed a reaction product of a phytosterol with fatty acids containing 2-22 carbon atoms. [*Id.* at 8]. The Examiner then baldly concluded that the "[i]nstant claims are a selection of prior art teachings." [*Id.*].

The rejection is predicated on the Examiner's conclusion that the disclosure of fatty acids containing C_{2-22} carbon atoms somehow identifies or suggests EPA and DHA. As appears, the sole basis for the Examiner's conclusion that the disclosure of C_{2-22} fatty acids suggests EPA and DHA is that these specific compounds "would have been obvious."

> ***It would have been obvious*** to one skilled in the art to prepare additional beneficial composition by selecting any fatty acids for example, docosahexaenoic acid and eicosahexaenoic acid from fatty acid 2-22 carbon atoms taught by the prior art. There has been ***ample motivation*** provided by the prior art to prepare the instant invention. Instant compositions would have been obvious at the time of the invention. The subject as instantly claimed would have been obvious to one at the time of the invention. (emphasis added) [*Id.*].[5/]

It is respectfully submitted that the Examiner misconstrued the specificity of the teachings of Mitchell and Miettinen. As the Examiner acknowledged, neither Mitchell

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5/ See note 1 *supra*.

nor Miettinen specifically disclose EPA or DHA. But, even though Mitchell expresses a preference for C_{18-20} fatty acids, the Examiner ignored clear disclosure in Mitchell suggesting that ***any*** fatty acid could be used to make the steroid vitamin supplements:

> Although **fatty acids having less than 18 carbon atoms ... or more than 20 carbon atoms ... may be used,** it has been found that phytosterol esters made from such fatty acids tend to have less utility in achieving the purposes of the present invention. (emphasis added) [Mitchell, Column 6, lines 9-15].

And, even within the preferred C_{18-20} family of fatty acids, Mitchell identifies and exemplifies only linoleic acid, linolenic acid and arachidonic acid. [See *Id.*, Column 5, lines 64-66 and Examples 1-75].

It is respectfully submitted that the Examiner also misinterpreted Miettinen. Miettinen broadly discloses that ***any*** vegetable oil or ***any*** C_{2-22} fatty acid may be used to obtain the phytosterol ester.

> A methyl ester mixture of the fatty acids of ***any*** vegetable oil can be used in the reaction .... ***any*** fatty acids which contain approx. 2-22 carbon atoms are usable. (emphasis added) [Miettinen, page 6, lines 30-34]
>
> * * * *
>
> Instead of a mixture of rapeseed oil fatty acid esters it is possible to use ... fatty acids which contain approximately 2-22 carbon atoms. [*Id.*, page 10, lines 20-24].

In short, Miettinen does not disclose a particular fatty acid. Rather, Miettinen identifies "any" oil and "any" C_{2-22} fatty acid in general and rapeseed oil in particular as a source of fatty acids. The Examiner did not identify any disclosure from Mitchell or Miettinen that would suggest using EPA or DHA as the source of the fatty acid component of a phytosterol ester as claimed. Nor did the Examiner even attempt to reconcile the apparent conflict between the narrow preferred range of fatty acids

disclosed in Mitchell (C_{18-20}) and its disclosure that fatty acids with less than 18 or more than 20 carbon atoms have less utility and the broad teachings of Miettinen that any C_{2-22} fatty acid may be used. Nor did the Examiner attempt to reconcile the fact that DHA, a 22 carbon atom fatty acid falls outside the preferred Mitchell range.

Accordingly, the rejection is left with two disclosures that recite conflicting ranges of preferred fatty acids, that do not recite either of the two claimed fatty acids and that provide no suggestion or motivation to select the two claimed fatty acids. At bottom, the Examiner is reduced to relying on the bald assertions that EPA and DHA "would have been obvious" and that "ample motivation" has been provided by the prior art. [Paper No. 17 at 8].

In sum, the Examiner failed to identify in Rejection 2 where in Mitchell and Miettinen there is a disclosure that would have suggested or motivated one to use EPA or DHA. Indeed, the Examiner failed to explain why one would even consider DHA in view of Mitchell's disclosure that fatty acids having more than 20 carbon atoms have less utility.

Thus, the rejection is factually deficient and cannot stand for this reason as well. *See Saceman*, 27 USPQ2d at 1474; and *Porter*, 25 USPQ2d at 1147. Moreover, it was the Examiner's burden to identify disclosures from Mitchell or Miettinen or technical reasoning that would have filled the acknowledged gap in these documents. This the Examiner did not do. The use of "would have been obvious" or "ample motivation" is not a substitute for the required factual showing of EPA or DHA or a disclosure that is sufficient to have suggested or motivated one skilled in the art to have selected EPA or DHA as claimed. Here, the Examiner failed to identify on what basis one would have

concluded that EPA and DHA would have been obvious choices based on Mitchell or Miettinen or where the alleged "ample motivation" comes from. In the absence of such evidence, the rejection is deficient and must be reversed.

POINT V

REJECTIONS 1 AND 2 IMPROPERLY RELIED ON A GENUS AS A DESCRIPTION OF TWO SPECIES – EPA AND DHA

Another error is that the Examiner failed to fill the acknowledged gap left by the cited documents with respect to the lack of any disclosure of a phytosterol ester made from EPA or DHA. The Examiner acknowledged that neither Miettinen nor Mitchell disclose EPA or DHA, thus Rejection 2 is completely lacking in a reference that discloses or suggests claims 1-4, 24 and 25 as a whole. And, the Examiner failed to explain why Kamarei is properly combinable with Mitchell and Miettinen – and, as set forth *supra*, it is not properly combinable – thus, Rejection 1 is also devoid of a reference that discloses or suggests claim 8 as a whole. Accordingly, Rejections 1 and 2 are factually deficient and must be reversed for this reason as well.

In Rejection 2, the Examiner's sole basis for rejecting claims 1-4, 24 and 25 is that "it would have been obvious" to use EPA and DHA based on fatty acids containing 2-22 carbon atoms "taught by the prior art." [*See* Paper No. 17 at 6]. The Examiner's unstated rationale for this conclusion appears to be that the genus of C_{2-22} fatty acids render obvious two species - EPA and DHA. Without more, however, this basis for rejection is deficient.

As is well settled, the disclosure of a genus does not render a species or a subgenus obvious. *In re Jones*, 21 USPQ2d 1941, 1944 (Fed. Cir. 1992) ("Conspicuously missing from this record is any *evidence*, other than the PTO's

speculation (if it be called evidence) that one of ordinary skill in the herbicidal art would have been motivated to make the modifications of the prior art salts necessary to arrive at the claimed 2-(2'-aminoethoxy) ethanol salt.... We conclude that the PTO did not establish a *prima facie* case of obviousness."); *In re Baird*, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) ("***The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious***.... While the Knapp formula unquestionably encompasses bisphenol A when specific variables are chosen, there is nothing in the disclosure of Knapp suggesting that one should select such variables.") (emphasis added); *Ex parte Tomko*, 2004 WL 77393, *2 (BPAI 2004) (unpublished) (Board reversed a §103 rejection of a claim to compounds containing a neopentylene phosphonate moiety in view of a prior art reference (Grey) teaching vinyl phosphanates, even though the claimed phosphonate was a member of the genus defined by the prior art reference.).

Here, the rejection is rooted in the Examiner's unsupported assertions that the claimed invention is nothing more than "a selection of prior art," that "it would have been obvious" to select EPA and DHA based on the teaching of C_{2-22} fatty acids in the "prior art," and that the prior art provides "ample motivation" apparently to go from C_{2-22} fatty acids to the specific C_{20} (EPA) and C_{22} (DHA) fatty acids that are claimed. [Paper No. 17 at 8]. The problems with this rejection are numerous.

First, the rejection does not even identify which piece of "prior art" supports its various assertions. Is the "prior art" in the rejection referring to Mittinen, to Mitchell, to both, or to some other piece of prior art that has not been made of record? Appellants should not have to guess at the source of the alleged "prior art."

Next, the rejection fails to identify with specificity what evidence supports the conclusion that there is "ample motivation" in the art to go from C_{2-22} to EPA and DHA. Although it is not our burden, we note that there is no disclosure in either Miettinen or Mitchell that would lead one from the broadly disclosed genus of fatty acids to EPA and DHA specifically.

Mitchell teaches that ***any*** fatty acid may be used to make the steroid and hormone intermediates, although C_{18-20} fatty acids are disclosed to have more utility. Mitchell specifically identifies "linolenic acid" (C_{18}, ω-3), "linoleic acid" (C_{18}, ω-6) and "arachindonic acid" (C_{20}, ω-6) as examples of preferred C_{18-20} fatty acids. Mitchell does not appear to express a preference for ω-3 vs. ω-6 fatty acids. Nor does Mitchell disclose or suggest EPA (C_{20}, ω-3) or DHA (C_{22}, ω-3). In fact, Mitchell suggests that DHA, a C_{22} fatty acid would have less utility than the preferred C_{18-20} fatty acids.

Miettinen is likewise of no help to the Examiner. Miettinen broadly discloses the use of "any" vegetable oil, as well as "any fatty acid which contain approx. 2-22 carbon atoms." [Miettinen, page 6, lines 30-34]. The Examiner did not identify a single specific fatty acid identified by Miettinen. Nor did the Examiner identify what disclosure in Miettinen would have led one to the claimed EPA and DHA. At bottom, the Examiner failed to identify any evidence to support her rejection.

And, the rejection completely ignores clear precedent that something more than a broad recitation of a generic formula is required to render obvious a species or subgenus encompassed by a generic formula. At best, the rejection points to a teaching of C_{2-22} fatty acids, but it fails to take the next step and identify where in the

"prior art" there is a suggestion to go from C_{2-22} to the specific C_{20} (EPA) and C_{22} (DHA) fatty acids as claimed.

In sum, it is respectfully submitted that each of the deficiencies noted above alone are sufficient to render Rejection 2 infirm - together, they compel its reversal. We also note that in the absence of any explanation of why one would combine Kamarei with Mitchell and Miettinen, Rejection 1 suffers from the same infirmities as Rejection 2 and should be reversed for these reasons as well.[6/]

POINT VI

THE EXAMINER NEVER ADDRESSED, MUCH LESS DEMONSTRATED THAT CLAIMS 24 AND 25 WOULD HAVE BEEN OBVIOUS

Another error is that the Examiner completely ignored claims 24 and 25, and thus, failed to engage in the mandatory analysis handed down by the Supreme Court and adopted as PTO policy. For example, the rejection failed to consider claims 24 and 25 as a whole. The rejection failed to identify the differences between claims 24 and 25 and the cited documents. And, the rejection failed to engage in any analysis relating to whether the inventions recited in claims 24 and 25, as a whole, would have been obvious. That was error. *See Graham v. John Deere Co.*, 383 US 1, 17-18, 148 USPQ 459, 467 (1966); and MPEP §2141 at 2100-115 ("Office policy is to follow *Graham v. John Deere Co.* in the consideration and determination of obviousness under 35 USC

6/ With respect to Rejection 1, we further note that Kamarei discloses that although EPA was observed to lower serum triglyceride levels, it was also observed to increase bleeding time and decrease platelet aggregation. [Kamarei, Column 2, lines 52-59]. Thus, even if Kamarei is properly combinable with Mitchell and Miettinen, which it is not, it teaches away from using EPA because of the adverse side effects. *See In re Rosenberger*, 156 USPQ 24, 26 (CCPA 1967) (To do what the prior art discourages is the "antithesis of obviousness."); and *In re Buehler*, 185 USPQ 781, 786-787 (CCPA 1975) ("Appellant's claimed method, however, involves doing what Clark (the cited prior art) tries to avoid .... This is the very antithesis of obviousness.").

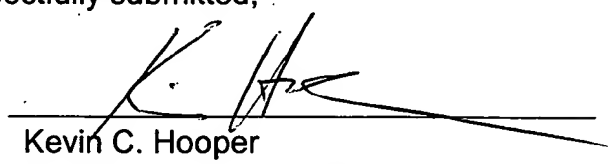
§103."); and *Ex Parte Roller*, 2004 WL 45458, *2 (unpublished) (BPAI 2004) ("In rejecting claims under 35 USC §103, it is incumbent upon the Examiner to establish a factual basis to support the legal conclusion of obviousness. In doing so, the Examiner is expected to make the factual determinations set forth in *Graham v. John Deere Co.*, and to provide a reason why one having ordinary skill in the art would have been led to modify the prior art or to combine prior art references to arrive at the claimed invention.") (citations omitted).

The Examiner did not acknowledge the specific physical properties of the phytostanol ester (*i.e.*, that it is liquid at temperatures from -20° to 20°C) recited in claim 24. Nor did the Examiner acknowledge that the compound of claim 25 was produced from a reaction of EPA or DHA with a mixture of phytosterol and phytostanol. The Examiner made no findings with respect to the phase (*i.e.*, solid, liquid, or gas) of the ester between -20°C to 20°C disclosed in Mitchell and Miettinen. Nor did the Examiner make any findings with respect to the nature of the esters formed from the reactions described in Mitchell and Miettinen and the nature of the claimed compound recited in claim 25. And, the Examiner made no finding with respect to why one skilled in the art would have believed that the compounds recited in claims 24 and 25, as a whole, would have been obvious in view of the disclosures of Miettinen alone, or in combination with, Mitchell. For this additional reason, the rejection of claims 24 and 25 should be reversed.

CONCLUSION

For all of the foregoing reasons, it respectfully is submitted that the Examiner has failed to make out a *prima facie* case of obviousness and hence Rejection 1 (of claim 8) and Rejection 2 (of claims 1-4, 24, and 25) should be reversed.

Respectfully submitted,

By: 

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APPENDIX I

1. A phytosterol ester compound produced from a reaction of a phytosterol with eicosapentaenoic acid or docosahexaenoic acid, said compound being liquid at temperatures from about -20°C to about 20°C.

2. A composition according to claim 1 wherein the phytosterol is selected from the group consisting of beta-sitosterol, stigmasterol, campesterol, and mixtures thereof.

3. A composition according to claim 2 wherein the phytosterol is selected form the group consisting of beta-sitosterol, stigmasterol, and mixtures thereof.

4. A composition according to claim 3 wherein the phytosterol is beta-sitosterol.

8. A composition comprising an admixture of the compounds (a) and (b) wherein (a) is a phytosterol ester compound produced from a reaction of a phytosterol with eicosapentaenoic acid or docosahexaenoic acid; and (b) is a second ester which is the product of an esterification reaction between a phytosterol and/or a phytostanol and (i) a fatty acid having less than 18 or more than 22 carbon atoms and at least three carbon-carbon double bonds and/or; (ii) a fatty acid having from 18 to 22 carbon atoms and less than three carbon-carbon double bonds.

24. A phytostanol ester compound produced from a reaction of a phytostanol with eicosapentaenoic acid or docosahexaenoic acid, said compound being liquid at temperatures from about -20°C to about 20°C.

25. A compound produced from a reaction of eicosapentaenoic acid or docosahexaenoic acid with a mixture of phytosterol and phytostanol, wherein the phytosterol is selected from the group consisting of beta-sitosterol, stigmasterol, campesterol, and mixtures thereof; and the phytostanol is selected from the group consisting of campestanol, beta-sitostanol, and mixtures thereof.